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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/539,169

06/14/2005

Frank Brady

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EXAMINER

PERREIRA, MELISSA JEAN

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

04/17/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/539,169	<b>Applicant(s)</b> BRADY ET AL.	
	<b>Examiner</b> Melissa Perreira	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 2,3 and 9-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 4-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/25/05; 6/14/05</u>  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of group I, claims 1-8, and the species of X= $I^+$  in the reply filed on 3/2/09 is acknowledged.
2. Claims 2,3 and 9-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups II and III there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/2/09.
3. The selected species,  $I^+$ , was not found in the prior art and thus the search was expanded to include the species  $R^{11}SnR^{12}$  of group I and therefore the claims 6 and 7 were examined on their merits

### *Claim Objections*

4. Claim 8 is objected to because of the following informalities: The instant claim 1 to which claim 8 depends does not contain the 18-F labeled tracer of formulas IIa, IIb and IV but does recite the 18-F labeled tracer labeled of formula II. Appropriate correction is required.
5. Claim 1 is objected to because of the following informalities: the instant claim does not end in a period. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. All "X" groups, which promote nucleophilic substitution at a specific site, of the instant claim wouldn't be expected to function in the same way as they will have different electrophilicity and the leaving group is important for successful nucleophilic substitution reactions. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1 and 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. It is unclear as to which solid support and linker is required as they are not identified in the instant claims.

10. Claim 8 recites the limitation "IIa, IIb or IV" in regards to claim 1. There is insufficient antecedent basis for this limitation in the claim. The instant claim 1 to which claim 8 depend does not contain the 18-F labeled tracer labeled formulas IIa, IIb or IV but does recite the 18-F labeled tracer labeled of formula II.

11. Claims 1,4 and 6 recite the limitation "the resultant compound". There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

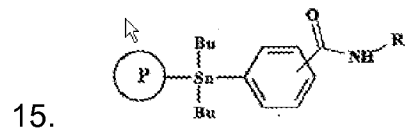
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al. (WO02/070020) in view of Stevens et al. (WO01/14354) and Scheler (US 4,540,648) and further in view of Shuttleworth et al. (Synthesis **1997**, 1217-1239).

14. Hunter et al. (WO02/070020) discloses the use of polymer-bound/solid support precursors (below) for the preparation of radiolabeled tracers/radiolabeled haloaromatics X-R-Y where X may be <sup>18</sup>F, R is aryl or heteroaryl, Y is amino, alkylamino, etc. (abstract; p1, especially lines 11-20 and 27-29; p3, lines 7-14; fig 6). The radiolabeled compounds are obtained via site-specific destannylation chemistry of

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the polymer-bound/solid support precursors where  $\text{Bu}_2\text{Sn}$  encompasses the group that promotes nucleophilic substitution, X, of the instant claims (p2, lines 1-15) and the polymer for the solid support, P, is a polystyrene (claim 13). The polymer-supported radiopharmaceutical precursors have chemical stabilities unusually greater than their non-supported counterparts without any particular precautions being taken, with greater shelf life (p3, lines 23-25). The preparation of radiolabeled compounds via polymer-bound/solid support systems involves treating the insoluble polymeric precursor compound with a radioisotope and an oxidant which releases radiolabeled compounds into solution and allows for purification of insoluble polymeric side-product via filtration to generate pure material (p3, lines 15-22).



16. Hunter et al. does not disclose a benzothiazole R group or of a linker between the solid support and the dialkyltin group.

17. Stevens et al. (WO01/14354) discloses the process for the production of  $^{18}\text{F}$ -substituted benzothiazoles for use in PET via site-specific destannylation chemistry with  $^{18}\text{F}$  acetyl hypofluorite (p5, lines 3-17; examples 44 and 45 including scheme).

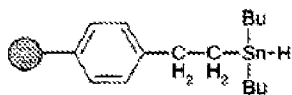
18. Scheler (US 4,540,648) discloses a benzothiazole/light sensitive compound linked to a solid support/film (i.e. polystyrene) via a coupler component (abstract; column 3, lines 25+; column 7, lines 5-11 and 60-66; claim 1). The polystyrene solid support encompasses the solid support of the disclosure as evidenced in the specification p6, lines 1-8.

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19. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute the benzothiazole of Stevens et al. for the heteroaryl group of Hunter et al. and thus radiolabel a benzothiazole (derivative) with an  $^{18}\text{F}$  radioisotope via the polymer-bound/solid support of Hunter et al. as both disclosures teach of radiolabeling a heteroaryl group with  $^{18}\text{F}$  via site-specific destannylation chemistry. The results would be predictable and advantageous, such as a rapid and clean preparation of  $^{18}\text{F}$ -substituted benzothiazoles PET agents (Stevens et al. p5, lines 3017) via a simplified purification/filtration step (Hunter et al., p3, lines 15-22). It would have been obvious to one ordinarily skilled in the art to attach a benzothiazole (derivative) to the polystyrene solid support (Hunter et al.) as Scheler teaches that benzothiazole may be linked to a polystyrene solid support via a coupler.

20. In regards to the linker between the solid support and dialkyltin X group:

21. Shuttleworth et al. (Synthesis **1997**, 1217-1239) discloses that solid phase synthesis has been known since 1963 and has continued to receive steadfast attention due to the ease of purification via filtration (p1217, paragraphs 2 and 3). The quest for environmentally friendly organic synthesis has driven the use of solid phase synthesis (p1218, paragraph 2). Polystyrene dialkyltin support systems with a linker (below) are known in the art (p1227, **37**).



22.

**37**

23. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute/try the polystyrene dialkyltin support systems of Hunter et al. for other polystyrene containing support systems, such as taught by Shuttleworth et al. for the process for the production of  $^{18}\text{F}$ -substituted benzothiazoles (of the combined disclosures above). Both type of polystyrene containing support systems are known in the art and contain a dibutyltin moiety and the results of such a substitution would give predictable results, such as a group that promotes nucleophilic substitution for site-specific destannylation chemistry.

### ***Conclusion***

No claims are allowed at this time. The species,  $\text{I}^+$ , was not found in the prior art and is objected to for depending on a rejected base claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/

Examiner, Art Unit 1618